

## REMARKS

Claims 1-3, 10-16 and 45 remain before the Examiner for reconsideration. Claims 4-9 and 17-44 have been canceled without prejudice. Claims 3, 13, 15 and 16 have been amended. The amendments to Claims 3, 13, 15 and 16 are set forth in an Appendix hereto in which additions to the claims are indicated by underling in deletions from the claims are marked by bracketing.

In the Office Action dated February 12, 2002, the Examiner made the restriction requirement set forth in the Office Action of September 20, 2001 final. In response thereto, Applicants have canceled without prejudice Claims 4-9 and 17-44.

The Examiner further indicated that the "drawings filed with the application are acceptable for examination and are approved by the PTO draftsman."

The Examiner objected to the abstract of the disclosure asserting that "it is too long." Applicants respectfully traverse the Examiner's objection as the original Abstract was neither longer the 250 words nor longer than 25 lines of text. However, Applicants have amended the Abstract to shorten it.

The Examiner rejected Claims 3, 13, 15 and 16 under 35 U.S.C. Section 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention." Specifically, the Examiner asserted that:

- A. Claims 3 and 13 lack clear antecedent basis for the terms 'the first tagged compounds' and 'the second tagged compounds' (emphasis added). The claims from which these claims depend refer to 'the first tagged compound' and the second tagged compound'.
- B. Claim 15 lacks antecedent basis for the terms 'first fluorous tagging moiety' and 'second fluorous tagging moiety.' The claims from which this claim depends (claim 14) has no recitation of this terminology whatsoever.
- C. Claim 16 lacks antecedent basis for the terms 'the first tagged compounds' and 'the second tagged compounds.' The claims from

which this claim depends (claims 14 and 15) have no recitation of this terminology whatsoever.

Applicants have amended Claims 3, 13, 15 and 16 to obviate the Examiner's rejection. The amendments to these claims are inherent in the claims as originally filed. The amendments do not affect the coverage of the claims, including any equivalents.

The Examiner rejected Claim 45 under 35 U.S.C. Section 102(b) "as being anticipated by Still et al (US 5,565,324).." Specifically, the Examiner has asserted that:

Still et al discloses 'encoded combinatorial chemistry' (See Abstract). Various tags are used as markers to identify compounds present in a chemical library (see column 3, lines 5-45). The reference discloses that N identifiers can uniquely encode  $2^N$  different compounds (column 3, lines 9-31). Specifically, the reference discloses that 'differentiation of tags can be achieved with physical differences, e.g. ... chromatographic retention time using gas or liquid chromatography (see column 26, lines 63-67; also column 7, lines 32-52). Still et al discloses changing the chemical nature of the tag to achieve a 'desired separation' (column 27, lines 1-31).

Applicants respectfully traverse the Examiner's rejection.

Still et al. discloses the attachment of an identifier molecule or molecules to a solid support upon which a compound is being synthesized. The tags are used to identify a particular event, typically a chemical synthesis step. See, for example, Col. 3, lines 5-15. The identifying molecules can be used to identify or distinguish between different support, but cannot be used to separate such solid supports or the compounds being synthesized thereon.

The identifying molecules can be cleaved from the solid support via a cleavable moiety. See, for example, Col. 3, lines 35-39. The identifying molecule(s) can be removed from the solid supports or beads via, for example, reductive, oxidative, thermolytic, hydrolytic or photolytic conditions.. See, for example, Col. 25, lines 61-65 and Col. 26, lines 57-62. Only once the tags of Still et al. are removed from the solid supports, can such tags or identifying molecules be differentiated or even separated "with physical differences, e.g., molecular weight of the tags or chromatographic retention time

using gas or liquid chromatography.” Col. 26 lines 62 – Col. 27, line 9.. Although the identifiers of Still et al can be used to distinguish differently tagged solid supports, it is not possible to separate the tagged solid supports of Still et al based upon differences in the identifying or tagging molecules. Thus, it is not possible to in the method of Still et al to separate a first tagged compound into a predetermined fraction from a mixture including at least the second tagged compound using a separation technique based upon differences between a first tagging moiety and a second tagging moiety, as claimed in the present invention. The “desired separation” referenced at Col. 27, lines 1-31 of Still et al and cited by the Examiner is a separation of different identifying molecules and not solid supports and/or product compounds tagged with such molecules.

The Examiner rejected Claims 1 (in part), 2, 3, 10, 11-16 and 45 under 35 U.S.C. Section 1039a) “as being unpatentable over Still et al (US 5,565,324) in view of Curran et al (US 5,829,247). Specifically, the Examiner asserted that:

Still et al teaches ‘encoded combinatorial chemistry’ (See Abstract). Various tags are used as markers to identify compounds present in the chemical library (see column 3, lines 5-45). This reference teaches that N identifiers uniquely encode  $2^N$  different compounds (column 3, lines 9-31). Specifically, the reference teaches that ‘differentiation of tags can be achieved with physical differences, e.g. ...chromatographic retention time using gas or liquid chromatography (see column 26, lines 63-67; also column 7, lines 32-52). Still et al teaches changing the chemical nature of the tag to achieve a ‘desired separation’ (column 27, lines 1-31). This reads on the limitation of the instant claim 10.

Still et al lacks the specific teaching of using fluorous tags and fluorous reverse phase chromatography.

However, such tags and chromatographic methods were well established in the art at the time of filing. For example, Curran et al teach separation techniques where ‘organic/fluorous phase separation techniques are used to effect separations’ (see Abstract). These techniques are defined in column 3, line 35 – column 4, line 4 of the reference and read on claims 1, 2, 11, 12, 14 and 15. Reversed phase chromatography is specifically described, column 3, line 49 – column 4, line 4 (reading on claims 3, 13 and 16). Curran et al teach that these methods are preferred for separation (and synthesis) of combinatorial libraries (see column 8, line 50 – column 9, line 32).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the fluoruous tags and fluoruous reversed phase chromatography of Curran et al. in the method of tagging combinatorial libraries of Still et al. A person of ordinary skill in the art would have been motivated to do so in order to have preferable and facile means to separate and identify library compounds (see Curran et al, column 8, lines 12-32).

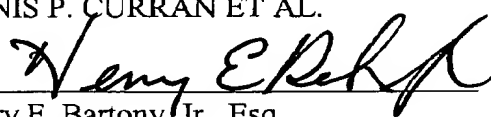
Curran et al does not overcome the deficiencies of Still et al set forth above. Once again, Still et al does not disclose or suggest separation of a first tagged compound from a second tagged compound using a separation technique based upon differences between a first tagging moiety and a second tagging moiety as claimed in the present invention. Curran et al discloses separation of a fluoruous tagged compound from an organic compound which does not include a fluoruous tag and does not disclose or suggest tagging of a plurality of compounds with different tagging moieties and subsequently separating the tagged compounds based upon differences between the nature of the tags.

In view of the above and remarks, the Applicants respectfully requests that the Examiner withdraw the objection to the Abstract, withdraw the rejections of the claims, indicate the allowability of the claims and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,

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## APPENDIX

### VERSION OF AMENDMENTS WITH MARKINGS TO SHOW REVISIONS

#### IN THE ABSTRACT:

Please delete the text of the Abstract and insert therefor the following:

A method of separating compounds that includes the steps of: tagging at least a first organic compound with a first tagging moiety to result in a first tagged compound; tagging at least a second organic compound with a second tagging moiety different from the first tagging moiety to result in a second tagged compound; and separating the first tagged compound from a mixture including the second tagged compound using a separation technique based upon differences between the first tagging moiety and the second tagging moiety. [Preferably, the separation technique is based upon difference in the fluoruous nature of the first tagged compound and the second tagged compound, differences in total charge between the first tagged compound and the second tagged compound, differences in size between the first tagged compound and the second tagged compound, and/or differences in polarity between the first tagged compound and the second tagged compound.] The present invention also provides a method for carrying out a chemical reaction including the steps of: tagging a plurality of compounds with different tagging moieties to create tagged compounds, conducting at least one chemical reaction on a mixture of the tagged compounds to produce a mixture of tagged products, and separating the mixture of tagged products by a separation technique based upon differences in the tagging moieties.

IN THE CLAIMS:

Please cancel without prejudice Claims 4-9 and Claims 17-44, which were withdrawn by the Examiner as a result of a restriction requirement.

Please delete the text of Claims 3, 13, 15 and 16 and insert therefor the following:

3. (Once Amended) The method of Claim 2 wherein the first tagged compound[s] and the second tagged compound[s] are separated using fluoruous reverse phase chromatography.

13. (Once Amended) The method of Claim 12 wherein the first tagged compound[s] and the second tagged compound[s] are separated using fluoruous reverse phase chromatography.

15. (Once Amended) The method of Claim 14 wherein [the] a first fluoruous tagging moiety and [the] a second fluoruous tagging moiety of the plurality of fluoruous tagging moieties differ in fluorine content or structure.

16. (Once Amended) The method of Claim 15 wherein [the] a first tagged compound[s] tagged with the first fluoruous tagging moiety and [the] a second tagged compound[s] tagged with the second fluoruous tagging moiety are separated using fluoruous reverse phase chromatography.